uniQure Announces Positive Topline Results from Pivotal Phase I/II Study of AMT-130 in Patients with Huntington's Disease

September 24, 2025

~ Pivotal study met primary endpoint; high-dose AMT-130 demonstrated statistically significant 75% disease slowing at 36 months as measured by cUHDRS compared to a propensity score-matched external control ~

~ High-dose AMT-130 also demonstrated statistically significant slowing of disease progression as measured by TFC, a key secondary endpoint, and favorable trends across additional clinical measures ~

~ Mean cerebrospinal fluid NfL levels were below baseline at 36 months ~

~ AMT-130 continued to be generally well-tolerated with a manageable safety profile ~

~ uniQure plans to submit a BLA in the first quarter of 2026, with anticipated U.S. launch later that year, pending approval ~

~ Investor conference call and webcast today at 8:30 a.m. ET ~

LEXINGTON, Mass. and AMSTERDAM, Sept. 24, 2025 (GLOBE NEWSWIRE) -- uniQure N.V. (NASDAQ: QURE), a leading gene therapy company advancing transformative therapies for patients with severe medical needs, today announced positive topline data from the pivotal Phase I/II study of AMT-130 for the treatment of Huntington's disease. The study met its prespecified primary endpoint, with high-dose AMT-130 demonstrating a statistically significant slowing of disease progression as measured by the composite Unified Huntington's Disease Rating Scale (cUHDRS) at 36 months compared to a propensity score-matched external control. The study also met a key secondary endpoint by achieving statistically significant slowing of disease progression as measured by Total Functional Capacity (TFC) at 36 months compared to a propensity score-matched external control.

"I am thrilled that this pivotal study of AMT-130 showed statistically significant effects on both cUHDRS and TFC at 36 months, supported by mean CSF NfL remaining below baseline," stated Sarah Tabrizi, M.D., FRCP, FRS, FMedSci, Ph.D., professor of clinical neurology, director of the University College London Huntington's Disease Center and joint head of the department of neurodegenerative disease. "I believe these groundbreaking data are the most convincing in the field to date and underscore potential disease-modifying effects in Huntington's disease, where an urgent need persists. These data indicate that AMT-130 has the potential to meaningfully slow disease progression – offering long-awaited hope to individuals and families impacted by this devastating disease."

In accordance with the prospectively defined statistical analysis plan aligned with, and submitted to, the U.S. Food and Drug Administration (FDA) for this pivotal Phase I/II study, uniQure analyzed clinical outcomes for 29 patients treated with AMT-130 (n=17 high dose; n=12 low dose) of which 12 patients per dose group had attained 36 months of follow up and were evaluated at that time point. Outcomes for each dose group were compared to a propensity score-matched external control drawn from the Enroll-HD natural history data set (n=940 for high dose; n=626 for low dose).

Topline 36-month efficacy results for patients receiving high-dose AMT-130 are as follows (data cutoff as of June 30, 2025):

- A statistically significant 75% slowing of disease progression as measured by cUHDRS (p=0.003), which met the primary endpoint of the study. Treated patients had a mean change in cUHDRS from baseline of -0.38 compared to a change of -1.52 for patients in the propensity score-matched external control.

- A statistically significant 60% slowing of disease progression as measured by TFC (p=0.033), which met a key secondary endpoint of the study. Treated patients had a mean change in TFC from baseline of -0.36 compared to a change of -0.88 for patients in the propensity score-matched external control.

- Favorable trends in other secondary endpoint measures of motor and cognitive function, including Symbol Digit Modalities Test (SDMT), Stroop Word Reading Test (SWRT) and Total Motor Score (TMS).

    - An 88% slowing of disease progression as measured by SDMT (p=0.057), with a mean change in SDMT from baseline of -0.44 compared to a change of -3.73 for patients in the propensity score-matched external control.

    - A 113% slowing of disease progression as measured by SWRT (p=0.002[1]), with a mean change in SWRT from baseline of 0.88 compared to a change of -6.98 for patients in the propensity score-matched external control.

    - A 59% slowing of disease progression as measured by TMS (p=0.174[1]), with a mean change in TMS from baseline of 2.01 compared to a change of 4.88 for patients in the propensity score-matched external control.

- A mean reduction from baseline in cerebrospinal neurofilament light protein (CSF NfL) of -8.2%. CSF NfL is a

well-characterized, supportive biomarker of neurodegeneration. Elevation in CSF NfL has been shown to be strongly associated with greater clinical severity of Huntington's disease.

The Company believes that the consistently favorable results in functional, motor and cognitive endpoints at 36 months observed in the high dose group, compared to the variable trends observed in the low dose group, reflect a dose-dependent response to AMT-130.

Various other supportive analyses of the results from the AMT-130 high dose treatment group, including those using a propensity score-weighted external control and comparisons to the TRACK-HD and PREDICT-HD datasets, were consistent with the primary analysis.

AMT-130 was generally well-tolerated, with a manageable safety profile at both doses. As of June 30, 2025, no new drug-related serious adverse events have been observed since December 2022. The most common adverse events in the treatment groups were related to the administration procedure, which all resolved.

"We are incredibly excited about these topline results and what they may represent for individuals and families affected by Huntington's disease," stated Walid Abi-Saab, M.D., chief medical officer of uniQure. "These findings reinforce our conviction that AMT-130 has the potential to fundamentally transform the treatment landscape for Huntington's disease, while also providing important evidence supporting one-time, precision-delivered gene therapies for the treatment of neurological disorders. Today's outcome reflects the tireless commitment of so many at uniQure, and I want to extend my deep gratitude to the team, as well as to the investigators, site personnel, patients and families who made this possible. We are eager to discuss the data with the FDA at our pre-BLA meeting expected later this year, with the goal of submitting a BLA in the first quarter of 2026."

AMT-130 has been granted Breakthrough Therapy designation and Regenerative Medicine Advanced Therapy (RMAT) designation from the FDA.

Investor Conference Call and Webcast Information

uniQure management will host an investor conference call and webcast today, Wednesday, September 24 at 8:30 a.m. ET. The event will be webcast under the Events & Presentations section of uniQure's website at https://www.uniqure.com/investors-media/events-presentations, and following the event a replay will be archived for 90 days. Interested parties participating by phone will need to register using this online form. After registering for dial-in details, all phone participants will receive an auto-generated e-mail containing a link to the dial-in number along with a personal PIN number to use to access the event by phone. If you are joining the conference call, please dial in 15 minutes before the start time.

About the Phase I/II Clinical Program of AMT-130

uniQure is conducting two multi-center, dose-escalating, Phase I/II clinical studies to explore the safety, tolerability, and exploratory efficacy signals of AMT-130 for the treatment of Huntington's disease. Based on interactions with the FDA, it was agreed that data from cohorts 1 and 2 in the Phase I/II studies could be compared to a propensity score-matched external control derived from the Enroll-HD natural history data set, under a prespecified statistical analysis plan, which may serve as the primary basis for a BLA submission.

In the U.S. study, a total of 26 patients with early manifest Huntington's disease were randomized to treatment (n=6 low dose; n=10 high dose) or an imitation (sham) procedure (n=10). Treated patients received a single administration of AMT-130 through MRI-guided, convection-enhanced stereotactic neurosurgical delivery directly into the striatum (caudate and putamen). The study consists of a blinded 12-month core study period followed by unblinded long-term follow-up of treated patients for five years. An additional four control patients crossed over to treatment. The European open-label Phase 1b/2 study of AMT-130 enrolled 13 patients with early manifest Huntington's disease (n=6 low dose; n=7 high dose).

A third cohort enrolled an additional 12 patients across sites in the U.S. and EU. This cohort was randomized to explore both doses of AMT-130 in combination with immunosuppression, using the current, established stereotactic administration procedure.

A fourth U.S. based cohort, evaluating high-dose AMT-130 in up to 6 patients with lower striatal volumes compared to those of patients enrolled in previous cohorts, is currently enrolling.

Additional details are available on www.clinicaltrials.gov (NCT0543017, NCT04120493)

About Huntington's Disease

Huntington's disease is a rare, inherited neurodegenerative disorder that leads to motor symptoms including chorea, behavioral abnormalities and cognitive decline resulting in progressive physical and mental deterioration. The disease is an autosomal dominant condition with a disease-causing CAG repeat expansion in the first exon of the huntingtin gene that leads to the production and aggregation of abnormal protein in the brain. Approximately 75,000 people have Huntington's disease in the U.S.[2], EU[3], and the UK[4], with hundreds of thousands of others at risk of inheriting the disease. Despite the clear etiology of Huntington's disease, there are currently no approved therapies to delay the onset or to slow the disease's progression.

About uniQure

uniQure is delivering on the promise of gene therapy – single treatments with potentially curative results. The approvals of uniQure's gene therapy for hemophilia B – an historic achievement based on more than a decade of research and clinical development – represent a major milestone in the field of genomic medicine and ushers in a new treatment approach for patients living with hemophilia. uniQure is now advancing a pipeline of proprietary gene therapies for the treatment of patients with Huntington's disease, refractory temporal lobe epilepsy, ALS, Fabry disease, and other severe diseases. www.uniQure.com

uniQure Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "establish," "estimate," "expect," "goal," "intend," "look forward to", "may," "plan," "potential," "predict," "project," "seek," "should," "will," "would" and similar expressions and the negatives of those terms. Forward-looking statements are based on management's beliefs and assumptions and on information available to management as of the date of this press release. Examples of these forward-looking statements include, but are not limited to, statements concerning: the potential clinical and functional effects of AMT-130; the Company's belief that AMT-130 has the potential to transform the Huntington's disease treatment landscape; the timing and outcome of regulatory

interactions with respect to the AMT-130 program, including the Company's expected pre-BLA meeting later this year and timing of the Company's planned BLA submission in the first quarter of 2026; and the Company's potential U.S. launch of AMT-130 in 2026. The Company's actual results could differ materially from those anticipated in these forward-looking statements for many reasons. These risks and uncertainties include, among others: risks related to the Company's Phase I/II clinical trials of AMT-130, including the risk that such trials will be unable to demonstrate data sufficient to support further clinical development or regulatory approval; the risk that more patient data become available that results in a different interpretation then the one derived from the topline data; risks related to the Company's interactions with regulatory authorities, which may affect the initiation, timing and progress of clinical trials and pathways to regulatory approval; whether the measurements that the Company is evaluating continue to be viewed as robust and sensitive measurements of disease progression; whether RMAT designation, Breakthrough Therapy designation, or any accelerated pathway, if granted, will lead to regulatory approval; the Company's ability to conduct and fund a Phase III or confirmatory study for AMT-130 if needed; the Company's ability to continue to build and maintain the infrastructure and personnel needed to achieve its goals; the Company's effectiveness in managing current and future clinical trials and regulatory processes; the Company's ability to demonstrate the therapeutic benefits of its gene therapy candidates in clinical trials; the continued development and acceptance of gene therapies; the Company's ability to obtain, maintain and protect its intellectual property; and the Company's ability to fund its operations and to raise additional capital as needed and on acceptable terms. These risks and uncertainties are more fully described under the heading "Risk Factors" in the Company's periodic filings with the U.S. Securities & Exchange Commission (SEC), including its Annual Report on Form 10-K filed with the SEC on February 27, 2025, its Quarterly Reports on Form 10-Q filed with the SEC on May 9, 2025 and July 29, 2025, and in other filings that the Company makes with the SEC from time to time. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements and, except as required by law, the Company assumes no obligation to update these forward-looking statements, even if new information becomes available in the future.

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[1] P-value is nominal.
[2] Yohrling G, et al. Neurology 2020;94(15 Suppl):954.
[3] Medina A, et al. Mov Disord 2022;37(12):2327–2335
[4] Furby H, et al. Eur J Neurol 2022;29(8):2249–2257.

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